AR201-13738

To: NCIC OPPT/DC/USEPA/US@EPA, ChemRTK HPV/DC/USEPA/US@EPA, Rtk Chem/DC/USEPA/US@EPA, Karen Boswell/DC/USEPA/US@EPA, nigel.j.sarginson@exxonmobil.com

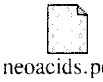
cc:

Subject: HPV comments on ExxonMobil's test plan for neoacids

Attached please find comments on ExxonMobil's test plan for the neoacids (C5-C28) category, submitted on behalf of a coalition of Animal Protection Organizations. Thank you for the opportunity to comment.

Sincerely,

Nicole Cardello, M.H.S.
Staff Scientist
PCRM
5100 Wisconsin Ave., N.W.
Suite 400
Washington, DC 20016
202-686-2210



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PCRM PHYSICIANS COMMITTEE FOR RESPONSIBLE MEDICINE
5100 WISCONSIN AVENUE, N.W. . SUITE 400
WASHINGTON, DC 20016
T: (202) 686-2210 • F: (202) 686-2216
PCRM@PCRM.ORG • WWW.PCRM.ORG

May 10, 2002

The Honorable Christine Todd Whitman
Administrator
U.S. Environmental Protection Agency
Ariel Rios Building
Room 3000, #1101-A
1200 Pennsylvania Ave., N.W.
Washington, DC 20460

Subject: Comments on ExxonMobil's HPV Test Plan for the Neoacids C5-C28 Category

Dear Administrator Whitman:

The following comments on ExxonMobil's test plan for the neoacid C5-C28 category are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These health, animal protection, and environmental organizations have a combined membership of more than nine million Americans.

The members of this category include neopentanoic acid (also known as 2,2-dimethyl propanoic acid or pivalic acid), C6-C8 neocarboxylic acids, neodecanoic acid neo fatty acids, and propanoic acid 2,2-dimethyl-, methyl ester. These compounds have uses in agricultural applications, pharmaceuticals, cosmetic preparations, polymers, and resins. ExxonMobil has developed a scientifically justifiable category, satisfying all criteria described in the EPA draft guidance document *Development of Chemical Categories in the HP V Challenge Program* (viewable at *http://www.epa.gov/chemrtk/categuid.htm).* ExxonMobil has presented data demonstrating similarity and trends in structure, physicochemical properties, and toxicity. However, ExxonMobil should expand this category to include the structurally similar HPV chemicals dccanoic acid and propanoic acid.

We are also concerned that ExxonMobil has proposed to conduct two *in vivo* genetic toxicity tests and one acute fish toxicity test. Not only are these tests inappropriate, given the available data and the understanding of the physicochemical properties of these chemicals, but they also violate the EPA guidance in the December *26, 2000, Federal Register* Notice (Vol. 65 No. 248) entitled, "Data Collection and Development on High Production Volume Chemicals" and the October 1999 Agreement among the EPA, industry, and health, animal protection, and environmental organizations.

The following terms of the October 1999 Agreement are violated by ExxonMobil's test plan for the neoacids C5-C28 category:

2. Participants shall maximize the use of existing and scientifically adequate data to

minimize further testing.

3. Participants shall maximize the use of scientifically appropriate categories of related chemicals and structure-activity relationships.
5. Participants are encouraged to use *in vitro* genetic toxicity testing to generate any needed genetic toxicity screening data, unless known chemical properties preclude its use.

Our three main comments on ExxonMobil's test plan are:

- ExxonMobil should have expanded the category to include structurally similar and isomeric HPV compounds.
- ExxonMobil should use existing data and/or in *vitro* genetic toxicity tests to address the genotoxicity endpoint.
- ExxonMobil should not conduct any in *vivo* toxicity tests on fish to test the neoacids, given their physicochemical properties and the availability ofnonanimal methods.

ExxonMobil should have expanded the category to include structurally similar and isomeric HPV compounds.

The development of chemical categories offers many advantages, including reduced testing and enhanced understanding of the relationship among structure, physicochemical properties, and toxicity. ExxonMobil should have included the HPV chemicals propanoic acid (CAS #79094) and decanoic acid (CAS #334-48-.5) in its category of neoacids, as they meet the criteria for inclusion. They are structurally very similar and have identical functional groups. In fact, decanoic acid andneodecanoic acid are isomers.

Increased coordination among HPV sponsors would reduce repetitive testing. Decanoic acid is being sponsored by the Soap and Detergent Association and through the ICCA by Crompton Corporation. Propanoic acid is being sponsored through ICCA and the SIDS program. We recommend that the sponsors communicate and cooperate, so as to maximize the use of available information on this category of chemicals.

ExxonMobil should use existing data and/or *in vitro* genetic toxicity tests to address the genotoxicity endpoint.

In its test plan, ExxonMobil states that there are no available genetic toxicity data on the neoacids in this category. To complete the hazard assessment of this chemical, ExxonMobil proposes to conduct the Ames assay on two chemicals, 2, 2-dimethyl propanoic acid and C9-C28 neofatty acids, to evaluate mutagenicity and the *in vivo* mouse micronucleus assay on those same chemicals to investigate clastogenicity. While we support the use of the bacterial mutation assay, we strongly recommend that ExxonMobil conduct OECD TG 473 *in vitro* mammalian cytogenetic test to examine chromosomal aberrations, rather than needlessly killing 120 mice to meet this endpoint. The October 1999 Agreement and the EPA *Federal Register* Notice specifically recommends the use of *in vitro* genetic toxicity data.

Furthermore, available data on the structurally similar HPV chemicals propanoic acid (also known as proprionic acid) and decanoic acid are available and could be used to characterize the potential genotoxic hazards posed by these chemicals. The available information should be used to fill data gaps under the HPV program.

Propanoic acid is also a fungicide and bactercide, already registered by the EPA to control fungi and bacteria in grains, hay, and grain storage areas. It is also found naturally in animal products and as a normal component of

metabolism in the human body and is considered Generally Recognized as Safe by the FDA. An EPA Reregistration Eligibility Document has been completed for propanoic acid. This document contains information that addresses each of the SIDS endpoints, including data indicating that propanoic acid is not mutagenic.'

Genotoxic properties of the food additive propanoic acid were analyzed using the Escherichia coli DNA repair assay, the SOS chromotest, the Salmonella/microsome mutagenicity test, the sister chromatid exchange test *in vitro* and the micronucleus test in *vivo*. All tests except the DNA repair assay with E. coli yielded negative results."

Another mouse micronucleus test has already been conducted with propanoic acid. The results were negative.'

Propanoic acid was also tested for its ability to induce sister chromatid exchanges in cultured human lymphocytes. Propanoic acid slightly elevated the incidence of sister chromatid exchange.[4]

Studies ofdecanoic acid are also available. Several commercially available C8 to C24 saturated and unsaturated fatty acids were assayed for cyclooxygenase-1 and cyclooxygenase-11 inhibitory and antioxidant activities. Most of the saturated fatty acids tested showed good antioxidant activity. Decanoic acid exhibited high inhibitory activities.'

ExxonMobil should not conduct any *in vivo* toxicity tests on fish to test the neoacids, given their physicochemical properties and the availability of nonanimal methods.

ExxonMobil has proposed to conduct an acute fish toxicity test with neofatty acids, C9-C13, despite the fact that adequate acute fish toxicity tests exist for three of the six chemicals in the category. This is sufficient to satisfy the endpoint under the HPV program. Additionally, the chemical mixture ExxonMobil has selected for testing has a pH range of 3.3 to 5.2. According to the EPA's December 26, 2000, *Federal Register* Notice (Vol. 65, No. 248) entitled *Data Collection and Development on High Production Volume (HPV) Chemicals,* no acute fish toxicity tests should be conducted for chemicals determined to have a log K_{ow} equal to or greater than 4.2. Rather, a chronic Daphnia study and algae plant toxicity study are sufficient and appropriate to meet the aquatic toxicity endpoint."

Expansion of the category would also provide additional ecotoxicity information on the neoacids. An acute toxicity study of propanoic acid a structurally similar compound, was conducted with Pimephales promelas (fathead minnow), and an LC50 of 4740 mg/l/96 hr (confidence limit 4390-5 120 mg/l) was observed. This was a flow-through bioassay with measured concentrations, 24.7 deg C, dissolved oxygen 6.1 mg/l, hardness 40.5 mg/l CaC03. alkalinity 42.2 mg/l CaC03, and pH 7.60.'

Moreover, given the availability ofnonanimal methods, any further testing on fish is inappropriate. ECOSAR, an established QSAR program that estimates toxicity to fish, invertebrates, and algae, could be used to further explore this endpoint. The EPA encourages the use of ECOSAR in its draft guidance document, *The Use of Structure-Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program* (viewable at *http://www.epa.gov/chemrtk/sarfinl1. htm).*

As described in previous comments, *in vitro* tests with the protozoan *Tetrahynzena* are frequently used as a measure ofaquatic toxicity in ecological risk assessments.* The biochemistry and physiology *of Tetrahymena* have been thoroughly investigated since the 1950s, and *Tetrahymena,* especially *T. pyriformis*, have been used for aquatic toxicity testing since the 1970s. Moreover, the genomics of the organism are currently being

elucidated. The *T. pyriformis* population growth test is quick, easy, cheap, and has great breadth." Both the *in vitro* TETRATOX assay as well as QSARs provide more humane, efficient methods to predict aquatic toxicity at the screening level. We have an ongoing dialogue with the EPA about the incorporation of these alternative, nonanimal methods into the HPV program, and we ask that ExxonMobil raise this issue with the EPA.

Thank you for the opportunity to comment. I look forward to your response on this important issue. I can be reached at 202-686-2210, ext. 302, or at *ncardello@pcrm.org*. Correspondence can be sent to my attention to PCRM, 5 100 Wisconsin Ave., N.W., Suite 400, Washington, DC 200 16.

Sincerely,

Nicole Cardello, M.H.S.
Staff Scientist

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